Sanofi	AVE0847
Mechanism of Action	Peroxisome proliferator-activated receptor α/γ (PPARα/γ)/nuclear receptor 1C1/1C3 (NR1C1/1C3) agonist http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=593&familyId=86 http://iuphar-db.org/DATABASE/ObjectDisplayForward?familyId=86&objectId=595 http://www.ncbi.nlm.nih.gov/gene/5465; http://www.ncbi.nlm.nih.gov/gene/5468
Overview	AVE0847 is an orally active, novel potent PPARα/γ agonist intended for the treatment of type 2 diabetes/insulin resistance and mixed dyslipidemia.
Safety/Tolerability	AVE0847 showed severe rhabdomyolysis at the maximum tolerated dose 0.5 mg, however, this dose was at least ten times above the dose that had maximum and strong triglyceride (TG)-lowering effects. The compatibility with statins with regards to rhabdomyolysis would have to be taken into account, requiring an early interaction program with statins. AVE0847 did not show free fatty acid (FFA)-lowering activity better than fenofibrate, which seems needed to lower blood glucose.
Additional Information	The target indication for AVE0847 is type 2 diabetes (T2DM). Preclinical results from animal models of T2DM demonstrated reductions of free fatty acids, blood glucose and HbA1c. The clinical relevance of PPARα agonists for glycemic control has not been demonstrated for any PPARα agonist so far. The relevance of the target remains to be shown.
Suitable for and Exclusions	The treatment in T2DM is chronic, requiring demonstration of chronic use safety. Carcinogenicity will have to be completed before the start of Phase 3.
Clinical Trials	Studies have been conducted in healthy volunteers only. Key results of single and multiple escalating dose, and food interaction studies were available since February 2005. AVE0847 was a back-up for AVE8134.
Publications	None